

SUPPLEMENTAL EXPERIMENTAL PROCEDURES

NSPC Isolation and Culture

NSPCs were prepared and cultured as described ([Brewer and Torricelli, 2007](#)). Passage 0 dissociated DIV (days-in-vitro) 0 cells were plated in ultra-low attachment 6-well plates (Corning) at a density of 4×10^5 cells per mL. On DIV4.5, cultures were dissociated into single cells, followed by nucleofection 2 h later. To induce bait DSB generation via GR-I-SceI, 10 μ M triamcinolone acetonide (TA, Sigma) was added on DIV5.5. Cells were collected for GRO-seq or HTGTS on DIV9. Replication stress was induced by addition of 0.5 μ M aphidicolin (APH, Sigma) for 72 h; cells were then fed with fresh medium, which resulted in reduction of APH concentrations to 0.25 μ M, and incubated for another 24 h before collection on DIV9.

Cas9:sgRNA-mediated DSB Induction

To induce Cas9:sgRNA-mediated DSBs, 5×10^6 dissociated DIV5 NSPCs were nucleofected with 5 μ g of Cas9:sgRNA expression vector by using the Mouse Neural Stem Cell Nucleofector reagent (VPG-1004, Lonza), as per manufacturer's instruction. Cas9:sgRNA expression vectors were constructed by ligating annealed oligonucleotides (see Table S7 for details) into *BbsI*-digested *pSpCas9(BB)* (Addgene plasmid 42230; [Cong et al., 2013](#)).

HTGTS

Libraries (fragment size 500 – 1,000 bp) were purified and sequenced (Illumina MiSeq). FASTQ output files were de-multiplexed, and unique reads aligned to genome build mm9/NCBI37 by Bowtie2 ([Langmead and Salzberg, 2012](#)) were processed through a custom HTGTS pipeline ([Frock et al., 2015](#)). See Table S7 for details on junction yield per experiment.

HTGTS Junction Enrichment Analysis

Unbiased, genome-wide identification of RDCs was performed by SICER ([Zang et al., 2009](#)) analysis of individual HTGTS libraries (excluding junctions within 5 Mb of the bait break-site) from untreated cells with the following parameters: *SICER-rb.sh species- mm9; redundancy threshold- 5; window- 30,000 bp; fragment size- 1; effective genome fraction- 0.74; gap size- 90,000 bp; E value- 0.1*. E-score cutoff was 50 for the break-site chromosome and 20 for all other chromosomes. SICER clusters had to be present in at least two biological replicate libraries to be considered RDCs. Identification of APH-induced DSB clusters was performed by SICER analysis of HTGTS data sets from control (DMSO) or treated (APH) cells using the following settings: *SICER.sh species- mm9; redundancy threshold- 5; window- 30,000 bp; fragment size- 1; effective genome fraction- 0.74; gap size- 90,000 bp; FDR- 0.01*. Only clusters with ≥ 1.5 -fold increase in junction density in individual libraries from APH-treated cells ($P < 0.05$, one-tailed unpaired t-test) were further considered. Among the shared clusters identified from different bait DSBs, only high-confidence clusters that showed ≥ 1.5 -fold increased translocation density over surrounding genomic areas of identical size and had been sampled ≥ 7 times were further considered.

For custom MACS-based, unbiased, genome-wide verification of significantly enriched junction clusters, HTGTS junctions were binned into 2.5-Mb regions and Poisson Lambda values (λ ; $\lambda = n_{junctions}/region\ size_{Mb}$) were computed for each bin (λ_r) and three surrounding regions: whole genome without break-site chromosome (λ_1), region extended by $1.5 \times (\lambda_2)$ and $2.5 \times (\lambda_3)$ on either side of bin center. P -values of enrichment of λ_r against the maximum value among λ_{1-3} were determined by Poisson distribution; $P < 0.05$ was considered significant. Significance of junction enrichment in replication stress-induced clusters was assessed as above but instead of

2.5-Mb bins, genomic coordinates of SICER clusters and surrounding regions were used to compute λ values.

Identification of Recurrent Translocations to Cas9:sgRNA Off-target Sites

Translocations between Cas9:sgRNA on- and off-target DSBs were identified as described (Frock et al., 2015) by MACS2 (Zhang et al., 2008; see also <http://github.com/taoliu/MACS>) with the following settings: `--keep-dup all --nomodel --extsize 2000 --llocal 10000000`. Hotspots ≥ 100 kb from the bait DSB break-site with an FDR-adjusted P -value threshold of 1×10^{-9} were considered translocations between Cas9:sgRNA on- and off-target DSBs if they shared $>30\%$ sequence with the on-target sgRNA-binding site, and formed focal translocations in plus and minus orientation in more than one biological replicate library.

Estimation of Translocation Rate and DSB Frequency

To estimate translocation frequency, we first determined the yield of unique junctions per amount of HTGTS library input DNA (assuming ~ 6 pg DNA per diploid mouse cell; 2.73×10^9 bp $\times 2$ (diploid) $\times 660$ (average MW per bp) $\times 1.67 \times 10^{-12}$ Da) by calculating the junction recovery rate:

$$\text{junction recovery rate (1 junction per } x \text{ genomes)} = \left[\frac{\text{input DNA (pg)}}{6 \text{ pg} \times n(\text{unique junctions})} \right]$$

Translocation rate (i.e., translocation number in a given genomic region per cell) was then calculated, factoring in the approximate fraction of cells with bait DSBs (0.5 for NSPCs; 0.8 for activated B cells):

$$\text{translocation rate} = \left[\frac{n(\text{junctions in region of interest}) \times \text{recovery rate}}{n(\text{cells with bait DSBs})} \right]$$

Multiplication of translocation rate $\times 100$ yielded the percentage of cells containing translocations within a given region. Frequencies of widespread DSBs were calculated based on the observed translocation rate on the *cis* (break-site) chromosome, excluding 500 kb on each side of the bait break-site. Frequencies of DSBs within *Lsamp* or *Npas3*, or within RDCs, were calculated based on the observed translocation rate of each of these categories on the break-site chromosome and multiplied by the total number of chromosomes (40) to derive an estimate of DSB number per cell. For direct comparison of DSB frequencies of *Lsamp* in NSPCs and *Bcl-6* in B cells (both of which are located on *Chr16* while the bait break-site is located on *Chr15*), translocation rates were directly equated to number of DSBs per cell.

DSB Repair Junction Signature Analysis

Junctional repair signatures in HTGTS libraries were analyzed at the nucleotide level by calculating the difference between end coordinate of the bait alignment and start coordinate of the prey alignment. In this calculation, a value of 0 corresponds to a "direct" junction, whereas negative values represent short nucleotide homologies or "microhomologies" (MHs); positive values indicate junctional nucleotide insertions.

SUPPLEMENTAL TABLES

Table S1. Relative HTGTS Junction Distribution, Related To Figure 1, 2, and 3.

Bait DSB	Genotype	Relative Distribution (%)				
		Break-site chromosome		Inter-chromosomal junctions		Npas3
<i>Chr12-sgRNA-1</i>	<i>Xrcc4-/- p53-/-</i>	61.39	>500 kb of break-site	31.00	1.13 #	0.42 #
<i>Chr12-sgRNA-1</i>	<i>Wild type</i>	49.83	4.94	45.24	0.21	0.16
<i>Chr12-sgRNA-2</i>	<i>Xrcc4-/- p53-/-</i>	58.86	8.41	32.73	2.66 #	0.22 #
<i>Chr16-sgRNA-1</i>	<i>Xrcc4-/- p53-/-</i>	52.36	7.40	40.24	0.28 #	1.90 #
<i>c-Myc-25xI-SceI</i>	<i>ATM-/-</i>	39.21	17.89	42.90	0.06	0.59 #
<i>c-Myc-25xI-SceI</i>	<i>Wild type</i>	61.66	6.16	32.18	0.07	0.99 #
<i>c-Myc-25xI-SceI</i>	<i>ATM-/- iABC*</i>	20.50	24.79	54.71	0.03	0.03

*Analysis of published *ATM*^{-/-} B cell HTGTS data ([Meng et al., 2014](#)). #Significant junction enrichment.

Table S2. Translocation and DSB Frequency Estimation, Related to Figures 1-6.

Translocation and DSB frequencies of the indicated classes of prey DSBs are shown. See *Supplemental Experimental Procedures* for details. *Junction number (in parentheses) within stated region; [†]Average junction number per RDC located on the break-site chromosome.

- DSB rates in *Lsamp* in NSPCs and DSBs in the AID off-target gene *Bcl-6* in activated B cells based on numbers of translocations between I-SceI-mediated bait DSBs on *Chr15* to prey DSBs (*Lsamp* or *Bcl-6*) on *Chr16*.

Genotype (Cell type)	Bait DSB	Input (µg)	Unique Junctions	Junction Number *	Translocation (% of cells)	DSBs per cell
<i>ATM</i> ^{-/-} (NSPC)	<i>c-Myc 25xI-SceI</i>	160	16,476	<i>Lsamp</i> (42)	0.5 %	0.005
<i>ATM</i> ^{-/-} (B cell [§])	<i>c-Myc 25xI-SceI</i>	80	42,751	<i>Bcl-6</i> (23)	0.1%	0.001

[§] *In vitro* activated B-cell HTGTS data from [Meng et al., 2014](#).

- Rates of widespread DSBs across the genome based on numbers of translocations between bait DSBs and prey DSBs on the *cis* chromosome (excluding junctions within 500 kb of bait break site).

Genotype (NSPCs)	Bait DSB	Input (µg)	Unique Junctions	Junction Number *	Translocation (% of cells)	DSBs per cell
<i>ATM</i> ^{-/-}	<i>c-Myc 25xI-SceI</i>	160	16,476	2,947 (<i>Chr15</i>)	35.8	14.3
<i>Xrcc4</i> ^{-/-} <i>p53</i> ^{-/-}	<i>Chr12-sgRNA-1</i>	100	20,000	1,586 (<i>Chr12</i>)	15.9	6.3
<i>Wild type</i>	<i>Chr12-sgRNA-1</i>	320	19,674	971 (<i>Chr12</i>)	9.9	3.9

3. Rates of DSBs within *Lsamp* or *Npas3* in the absence of induced replication stress, based on numbers of translocations between bait DSBs and prey DSBs within *Lsamp* or *Npas3* on the *cis* chromosome.

Genotype (NSPCs)	Bait DSB	Input (μg)	Unique Junctions	Junction Number *	Translocation (% of cells)	DSBs per cell
<i>Xrcc4</i> ^{-/-} <i>p53</i> ^{-/-}	<i>Chr12</i> -sgRNA-2	120	12,593	109 (<i>Npas3</i>)	1.7	0.7
<i>Xrcc4</i> ^{-/-} <i>p53</i> ^{-/-}	<i>Chr16</i> -sgRNA-1	120	19,798	151 (<i>Lsamp</i>)	1.5	0.6

4. Rates of RDC-gene-associated DSBs based on numbers of translocations between bait DSBs and RDCs on the *cis* chromosome.

Genotype (NSPCs)	Bait DSB	Input (μg)	Unique Junctions	Junction Number [†]	Translocation (% of cells)	DSBs per cell
<i>Xrcc4</i> ^{-/-} <i>p53</i> ^{-/-}	<i>Chr12</i> -sgRNA-1	75	40,755	177 (<i>Chr12</i>)	23.5 (27 RDCs)	9.4
Wild type	<i>Chr12</i> -sgRNA-1	70	11,304	47 (<i>Chr12</i>)	11.6 (14 RDCs)	4.7
<i>Xrcc4</i> ^{-/-} <i>p53</i> ^{-/-}	<i>Chr15-Myc</i> -sgRNA	75	23,959	158 (<i>Chr15</i>)	35.6 (27 RDCs)	14.2
Wild type	<i>Chr15-Myc</i> -sgRNA	70	13,911	57 (<i>Chr15</i>)	11.5 (14 RDCs)	4.6

Table S3. Supplied as a separate Excel file.

Table S4. HTGTS Junction Enrichment within Identified Replication Stress-sensitive Genes, Related to Figures 4, 5, and S3 and S4.

MACS-based HTGTS junction enrichment analysis against background λ in APH-treated *Xrcc4*^{-/-}*p53*^{-/-} samples as described in *Supplemental Experimental Procedures*.

Chr	Start	End	RefSeq ID	Gene	P value		
					Chr15 bait DSB	Chr12 bait DSB	Chr16 bait DSB
chr1	25,124,320	25,886,552	NM_175642	<i>Bai3</i>	3.63×10^{-2}	1.77×10^{-5}	2.84×10^{-3}
chr1	61,685,398	62,688,858	NM_001081050	<i>Pard3b</i>	2.85×10^{-4}	1.55×10^{-7}	1.56×10^{-3}
chr10	48,819,269	49,508,560	NM_001111268	<i>Grik2</i>	2.15×10^{-2}	2.42×10^{-7}	1.01×10^{-3}
chr12	38,607,291	39,359,997	NM_178681	<i>Dgkb</i>	1.38×10^{-2}	4.28×10^{-15}	8.87×10^{-3}
chr12	54,349,664	55,173,162	NM_013780	<i>Npas3</i>	6.62×10^{-6}	5.77×10^{-51}	1.57×10^{-5}
chr12	67,567,046	68,323,536	NM_001193266	<i>Mdga2</i>	1.38×10^{-2}	6.43×10^{-24}	9.00×10^{-5}
chr12	90,032,948	91,573,373	NM_001198587	<i>Nrxn3</i>	8.47×10^{-2}	3.6×10^{-14}	7.21×10^{-3}
chr14	117,324,519	118,378,751	NM_001079844	<i>Gpc6</i>	3.72×10^{-3}	6.21×10^{-6}	1.01×10^{-3}
chr15	30,102,348	30,959,098	NM_008729	<i>Ctnnd2</i>	4.62×10^{-15}	8.95×10^{-5}	1.75×10^{-4}
chr15	41,279,028	41,692,593	NM_001130166	<i>Oxr1</i>	9.78×10^{-6}	6.51×10^{-4}	1.47×10^{-3}
chr15	47,412,184	48,623,535	NM_001081391	<i>Csmd3</i>	1.96×10^{-51}	8.99×10^{-8}	2.05×10^{-4}
chr16	5,884,886	7,412,573	NM_021477	<i>Rbfox1</i>	5.75×10^{-2}	6.02×10^{-4}	1.95×10^{-19}
chr16	28,158,669	28,753,329	NM_010199	<i>Fgf12</i>	2.28×10^{-2}	4.44×10^{-3}	1.29×10^{-10}
chr16	66,655,666	67,621,153	NM_001145977	<i>Cadm2</i>	1.56×10^{-3}	6.24×10^{-6}	2.00×10^{-28}
chr17	90,432,984	91,492,142	NM_020252	<i>Nrxn1</i>	3.23×10^{-4}	6.73×10^{-9}	4.53×10^{-4}
chr18	71,413,285	72,510,723	NM_007831	<i>Dcc</i>	9.59×10^{-4}	3.10×10^{-7}	4.39×10^{-4}
chr19	30,638,977	31,839,523	NM_001013833	<i>Prkg1</i>	8.47×10^{-2}	2.12×10^{-5}	4.63×10^{-4}
chr4	97,248,634	97,785,567	NM_001122952	<i>Nfia</i>	6.98×10^{-4}	6.92×10^{-4}	2.77×10^{-4}
chr5	18,732,864	20,210,609	NM_001170746	<i>Magi2</i>	1.75×10^{-4}	5.48×10^{-5}	2.25×10^{-3}

<i>chr5</i>	141,717,488	142,689,745	NM_177879	<i>Sdk1</i>	7.58×10^{-3}	3.39×10^{-6}	2.26×10^{-5}
<i>chr6</i>	36,665,663	36,761,361	NM_008973	<i>Ptn</i>	1.01×10^{-2}	1.14×10^{-5}	7.38×10^{-3}
<i>chr6</i>	76,831,631	77,929,661	NM_001109764	<i>Ctnna2</i>	1.01×10^{-3}	4.54×10^{-7}	8.25×10^{-5}
<i>chr8</i>	15,892,545	17,535,385	NM_053171	<i>Csmd1</i>	7.47×10^{-4}	1.04×10^{-4}	4.61×10^{-4}
<i>chr8</i>	116,963,552	117,876,612	NM_019573	<i>Wwox</i>	7.94×10^{-3}	9.03×10^{-5}	1.18×10^{-2}
<i>chr8</i>	120,807,655	121,847,348	NM_019707	<i>Cdh13</i>	8.98×10^{-4}	6.08×10^{-9}	2.04×10^{-4}
<i>chr9</i>	28,803,549	29,770,714	NM_172290	<i>Ntm</i>	1.47×10^{-3}	1.80×10^{-5}	2.39×10^{-3}

Table S5. Translocation Junction Signatures of Replication Stress-induced RDC-genes.

Junctions from three to five independent experiments per bait DSB location and genotype were analyzed; total junction number analyzed per condition is listed in parentheses. Data represent mean and S.E.M. MH, microhomology.

Chr12-sgRNA-1 bait DSBs			
% of junctions	Wild type (n=416)	Xrcc4 ^{-/-} p53 ^{-/-} (n=1,312)	P-value (two-tailed unpaired t test)
Direct	42.8 ± 1.7	6.6 ± 1.1	4.2×10^{-4}
MH (1-10 bp)	57.2 ± 1.7	93.4 ± 1.1	4.2×10^{-4}
Chr15-Myc-sgRNA bait DSBs			
% of junctions	Wild type (n=406)	Xrcc4 ^{-/-} p53 ^{-/-} (n=825)	P-value (two-tailed unpaired t test)
Direct	37.3 ± 3.1	7.7 ± 1.2	1.6×10^{-5}
MH (1-10 bp)	62.7 ± 3.1	92.3 ± 1.2	1.5×10^{-5}

Table S6. Supplied as a separate Excel file.

Table S7. Detailed Information on HTGTS Libraries, Related to Figure 1-6 and Experimental Procedures.

1. sgRNA- and HTGTS-related oligonucleotide sequences. Bio, biotinylation. [#]Nucleotides used as linker sequences for cloning into *BbsI*-digested *pSpCas9(BB)* (Addgene plasmid 42230; Cong et al., 2013) are underlined.

*For details on LAM-HTGTS adapter sequences (I5, I7, P5, P7) see Frock et al., 2015.

sgRNA-RNA-related oligonucleotides		
Name	Sequence (5' > 3') [#]	sgRNA target coordinates (NCBI37/mm9)
Chr12-sgRNA-1 A	<u>CACC</u> ATTCCGCCAACCTCGAGAT	Chr12:13,000,844-
Chr12-sgRNA-1 B	<u>AAAC</u> ATCTCGAGGGTTGGCGGAAT	13,000,863
Chr12-sgRNA-2 A	<u>CACC</u> GCTGTCACTAGGAACGTTATC	Chr12: 61,485,370-
Chr12-sgRNA-2 B	<u>AAAC</u> GATAACGTTCTAGTGACAGC	61,485,390
Chr15-Myc-sgRNA A	<u>CACC</u> GCCCTATTCATCTGCGACG	Chr15: 61,819,136-
Chr15-Myc-sgRNA B	<u>AAAC</u> CGTCGCAGATGAAATAGGGC	61,819,155
Chr16 sgRNA-1 A	<u>CACC</u> GCTCCAACCTTAGCCCATC	Chr16: 31,462,937-
Chr16 sgRNA-1 B	<u>AAAC</u> GATGGGCTAAGGGTGGAGC	31,462,956
Chr16-sgRNA-2 A	<u>CACC</u> GATACGGCAAAGGACTAGTT	Chr16: 39,382,741-
Chr16-sgRNA-2 B	<u>AAAC</u> AACTAGTCCTTGCCGTATC	39,382,760
LAM-HTGTS Oligonucleotides		

Name	Sequence (5' > 3')
Bio- Chr12-sgRNA-1	Bio/CAGGTGCCAAGTTCTACCAACAAGC
Bio- <i>Chr12</i> -sgRNA-2	Bio/CTGCTTGACATTCAGCTATCTAAT
Bio- <i>Chr15-Myc</i> -sgRNA	Bio/CGAGCGTCACTGATAGTAGGGAGT
Bio- <i>Chr16</i> -sgRNA-1	Bio/AGGTACTACTGAGAGCTACCTC
Bio- <i>Chr16</i> -sgRNA-2	Bio/CTATGGAGTGACTGAAGCTAAATT

Oligonucleotides for nested-PCR (without Illumina I5 5'-adapter sequence*)

Name	Sequence (5' > 3')
PreCas <i>Chr12</i> -sgRNA-1	CCTCTAACATAAAAAGTGGAAAGTAGTT
PreCas <i>Chr12</i> -sgRNA-2	GCAAACACTGAAAGAGGCACCTGTGAG
PreCas <i>Chr15-Myc</i> -sgRNA	GCACCAACCAGAGCTGGATAACTCT
PreCas <i>Chr16</i> -sgRNA-1	GTTCCTAGCCGTGTGAATTGAGG
PreCas <i>Chr16</i> -sgRNA-2	GATAGTCGGGAAACGTTGGGATGC

2. sgRNA Off-target sites identified via HTGTS. Nucleotides conserved between on- and off-target loci are in red. PAM is underlined.

<i>Chr15-Myc</i>-sgRNA		
On-target	Off-target (identified by HTGTS)	Off-target locus
GCCCTATTCATCTGCGACG <u>AGG</u>	GCCCTATTCAC<u>CTGCAACA</u> GGG	<i>Chr11:78,738,291-78,738,310</i>
	ACCC<u>TTAACG</u>CAC<u>CTGCGACA</u> AGG	<i>Chr17:25,707,243-25,707,262</i>
<i>Chr12</i>-sgRNA-1		
On-target	Off-target (identified by HTGTS)	Off-target locus
ATTCCGCCAACCTCGAGAT <u>AGG</u>	CCC <u>ATCCCATCC</u> AT <u>CCC</u> GA GGG	<i>Chr12:112,278,690-112,278,709</i>
<i>Chr16</i>-sgRNA-1		
On-target	Off-target (identified by HTGTS)	Off-target locus
GCTCCAACCCTAGCCCATC <u>AGG</u>	GAAG<u>TTACAG</u>TT<u>CGCC</u>TGAT GGG	<i>Chr2:92,090,109-92,090,128</i>
<i>Chr16</i>-sgRNA-2		
On-target	Off-target (identified by HTGTS)	Off-target locus
CTGTGATAGTCGGGGAACGT <u>TGG</u>	A<u>AGGA</u>A<u>AGACT</u>G<u>AGCAAC</u>AC TGG	<i>Chr8:69,971,278-69,971,297</i>
	AG<u>GGACT</u>T<u>AGTAATAC</u>AGCAA <u>AGG</u>	<i>Chr15:94,741,284-94,741,303</i>

3. Summary of HTGTS junctions per experiment. NSPC genotypes, bait DSB site, name of experiment, corresponding junction number, and related Figures are listed.

***ATM-/- R26^{GR-I-SceI} c-Myc^{25xI-SceI}* (Figure 2C)**

Exp-A (6,667)
Exp-B (4,712)
Exp-C (2,182)
Exp-D (2,915)

***Xrcc4-/-p53-/- Chr12-sgRNA-1* (Figures 1B, 2A, 3A, S1B, S1C, and S5G)**

Exp-A (7,098)
Exp-B (4,628)
Exp-C (10,754)

Exp-D (9,664)

Xrcc4+/+p53-/ Chr12-sgRNA-1 (Figure S5G)

Exp-A (5,962)
Exp-B (7,443)
Exp-C (7,345)
Exp-D (11,147)

Wild type Chr12-sgRNA-1 (Figure S5G)

Exp-A (4,579)
Exp-B (2,382)
Exp-C (1,828)
Exp-D (2,883)
Exp-E (2,353)
Exp-F (2,216)
Exp-G (1,828)

Xrcc4-/-p53-/ Chr15-Myc-sgRNA (Figure S5G)

Exp-A (7,812)
Exp-B (4,593)
Exp-C (4,596)
Exp-D (4,930)

Xrcc4+/+p53-/ Chr15-Myc-sgRNA (Figure S5G)

Exp-A (5,176)
Exp-B (8,227)
Exp-C (8,367)
Exp-D (8,809)

Wild type Chr15-Myc-sgRNA (Figure S5G)

Exp-A (9,095)
Exp-B (3,338)
Exp-C (2,152)

Xrcc4-/-p53-/ Chr12-sgRNA-2 (Figure 3B)

Exp-A (4,266)
Exp-B (4,417)
Exp-C (3,910)

Xrcc4-/-p53-/ Chr16-sgRNA-1 (Figure 2B)

Exp-A (7,220)
Exp-B (6,836)
Exp-C (5,742)

Xrcc4-/-p53-/ Chr15-Myc-sgRNA (Figures 4, 5, S2-5)

DMSO, Exp-A (7,533)	APH, Exp-A (8,509)
DMSO, Exp-B (7,733)	APH, Exp-B (7,467)
DMSO, Exp-C (6,497)	APH, Exp-C (7,983)

Xrcc4-/-p53-/ Chr12-sgRNA-1 (Figures 4, 5, 7, S2-5)

DMSO, Exp-A (9,853)	APH, Exp-A (10,813)
DMSO, Exp-B (8,543)	APH, Exp-B (17,370)
DMSO, Exp-C (9,122)	APH, Exp-C (12,572)

Xrcc4-/-p53-/ Chr16-sgRNA-2 (Figures 4, 5, S2-6)

DMSO, Exp-A (6,202)	APH, Exp-A (4,438)
DMSO, Exp-B (5,799)	APH, Exp-B (3,787)
DMSO, Exp-C (5,678)	APH, Exp-C (4,495)

APH, Exp-D (6,114)

Wild type Chr15-Myc-sgRNA (Figures 6 and S5)

DMSO, Exp-A (3,450)	APH, Exp-A (4,276)
DMSO, Exp-B (3,406)	APH, Exp-B (3,486)
DMSO, Exp-C (2,005)	APH, Exp-C (1,979)
DMSO, Exp-D (2,833)	APH, Exp-D (1,476)
DMSO, Exp-E (2,826)	APH, Exp-E (2,694)

Wild type Chr12-sgRNA-1 (Figures 6 and S5)

DMSO, Exp-A (4,941)	APH, Exp-A (5,576)
DMSO, Exp-B (1,717)	APH, Exp-B (2,080)
DMSO, Exp-C (2,046)	APH, Exp-C (1,875)
DMSO, Exp-D (1,384)	APH, Exp-D (1,773)

SUPPLEMENTAL REFERENCES

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